

# TRAITÉ DE COOPÉRATION EN MATIÈRE DE BREVETS

## PCT

### RAPPORT PRÉLIMINAIRE INTERNATIONAL SUR LA BREVETABILITÉ

(chapitre I du Traité de coopération en matière de brevets)

(règle 44bis du PCT)

Référence du dossier du déposant ou du mandataire CP 61010PCT	POUR SUITE À DONNER		Voir le point 4 ci-dessous
Demande internationale no. PCT/FR2004/001470	Date du dépôt international (jour/mois/année) 11 June 2004 (11.06.2004)	Date de priorité (jour/mois/année) 11 June 2003 (11.06.2003)	
Classification internationale des brevets (8 <sup>e</sup> édition, sauf indication d'une #dition ant#rieure) Voir les informations pertinentes dans le formulaire PCT/ISA/237			
Déposant CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS)			

1. Le présent rapport préliminaire international sur la brevetabilité (chapitre I) est établi par le Bureau international au nom de l'administration chargée de la recherche internationale selon la règle 44bis.1.a).

2. Ce RAPPORT comprend un total de 14 feuilles, y compris la présente feuille de couverture.

Dans les feuilles jointes, toute référence à l'opinion écrite de l'administration chargée de la recherche internationale doit être entendue, à la place, comme une référence au rapport préliminaire international sur la brevetabilité (chapitre I).

3. Le présent rapport contient des indications relatives aux points suivants :

- |                                     |               |   |
|-------------------------------------|---------------|---|
| <input checked="" type="checkbox"/> | Cadre n° I    | Base de l'opinion   |
| <input checked="" type="checkbox"/> | Cadre n° II   | Priorité  |
| <input checked="" type="checkbox"/> | Cadre n° III  | Absence de formulation d'opinion quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle  |
| <input type="checkbox"/>            | Cadre n° IV   | Absence d'unité de l'invention  |
| <input checked="" type="checkbox"/> | Cadre n° V    | Déclaration motivée selon l'article 35.2) quant à la nouveauté, l'activité inventive et la possibilité d'application industrielle; citations et explications à l'appui de cette déclaration |
| <input type="checkbox"/>            | Cadre n° VI   | Certains documents cités  |
| <input checked="" type="checkbox"/> | Cadre n° VII  | Certaines irrégularités relevées dans la demande internationale   |
| <input type="checkbox"/>            | Cadre n° VIII | Certaines observations relatives à la demande internationale  |

4. Le Bureau international communiquera le présent rapport aux offices désignés conformément aux règles 44bis.3.c) et 93bis.1 mais pas avant l'expiration du délai de 30 mois à compter de la date de priorité (règle 44bis.2), sauf si le déposant a présenté une requête expresse à cet égard en vertu de l'article 23.2).

Bureau international de l'OMPI 34, chemin des Colombettes 1211 Geneva 20, Switzerland	Date d'établissement du présent rapport 01 May 2006 (01.05.2006)
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# PATENT COOPERATION TREATY

Translation

From the  
INTERNATIONAL SEARCHING AUTHORITY

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

To:

Date of mailing  
(day/month/year)

Applicant's or agent's file reference

**CP 61010PCT**

**FOR FURTHER ACTION**

See paragraph 2 below

International application No.

**PCT/FR2004/001470**

International filing date (day/month/year)

**11.06.2004**

Priority date (day/month/year)

**11.06.2003**

International Patent Classification (IPC) or both national classification and IPC

Applicant

**CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS)**

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☒ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☒ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/EP

Authorized officer

Facsimile No.

Telephone No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.  
☐ This opinion has been established on the basis of a translation from the original language into the following language \_\_\_\_\_, which is the language of a translation furnished for the purposes of international search (under Rule 12.3 and 23.1(b)).
2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material  
☐ a sequence listing  
☐ table(s) related to the sequence listing
  - b. format of material  
☐ in written format  
☐ in computer readable form
  - c. time of filing/furnishing  
☐ contained in the international application as filed.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

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Box No. II

Priority

1. ☐ The following document has not yet been furnished:

☐ copy of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(a)).

☐ translation of the earlier application whose priority has been claimed (Rule 43bis.1 and 66.7(b)).

Consequently it has not been possible to consider the validity of the priority claim. This opinion has nevertheless been established on the assumption that the relevant date in the claimed priority date.

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rules 43bis.1 and 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application  
☒ claims Nos. 9 (in part), 16

because:

- ☐ the said international application, or the said claims Nos. \_\_\_\_\_  
relate to the following subject matter which does not require an international preliminary examination (*specify*):

See supplemental sheet

- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. \_\_\_\_\_  
are so unclear that no meaningful opinion could be formed (*specify*):

- ☒ the claims, or said claims Nos. 9 are so inadequately supported  
by the description that no meaningful opinion could be formed.

- ☒ no international search report has been established for said claims Nos. 16

- ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form

☐ has not been furnished

☐ does not comply with the standard

the computer readable form

☐ has not been furnished

☐ does not comply with the standard

- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.

- ☐ See Supplemental Box for further details.

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Box No. V	Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement																					
1. Statement	<table><tbody><tr><td rowspan="2">Novelty (N)</td><td>Claims</td><td>1-8, 10-15, 17</td><td>YES</td></tr><tr><td>Claims</td><td>9</td><td>NO</td></tr><tr><td rowspan="2">Inventive step (IS)</td><td>Claims</td><td>1-8, 10-15, 17</td><td>YES</td></tr><tr><td>Claims</td><td>9</td><td>NO</td></tr><tr><td rowspan="2">Industrial applicability (IA)</td><td>Claims</td><td>1-15, 17</td><td>YES</td></tr><tr><td>Claims</td><td></td><td>NO</td></tr></tbody></table>	Novelty (N)	Claims	1-8, 10-15, 17	YES	Claims	9	NO	Inventive step (IS)	Claims	1-8, 10-15, 17	YES	Claims	9	NO	Industrial applicability (IA)	Claims	1-15, 17	YES	Claims		NO
Novelty (N)	Claims		1-8, 10-15, 17	YES																		
	Claims	9	NO																			
Inventive step (IS)	Claims	1-8, 10-15, 17	YES																			
	Claims	9	NO																			
Industrial applicability (IA)	Claims	1-15, 17	YES																			
	Claims		NO																			
2. Citations and explanations:	<p>1 Reference is made to the following documents in the present notification:</p> <p>D1: SUN J-S ET AL: "The influence of hydroxyapatite particles on osteoclast cell activities" JOURNAL OF BIOMEDICAL MATERIALS RESEARCH 15 JUN 1999 UNITED STATES, vol. 45, no. 4, 15 June 1999 (1999-06-15), pages 311-321, XP002305029 ISSN: 0021-9304</p> <p>D2: LANGSTAFF S ET AL: "Resorbable bioceramics based on stabilized calcium phosphates. Part II: evaluation of biological response" BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, vol. 22, no. 2, 15 January 2001 (2001-01-15), pages 135-150, XP004236387 ISSN: 0142-9612</p> <p>D3: ROVIRA A ET AL: "Colonization of a calcium phosphate/elastin-solubilized peptide-collagen composite material by human osteoblasts" BIOMATERIALS, ELSEVIER SCIENCE PUBLISHERS BV., BARKING, GB, vol. 17, no. 15, 1996, pages 1535-1540, XP004032703 ISSN: 0142-9612</p>																					

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Box No. V

Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

2 INDEPENDENT CLAIM 1

2.1 Document D1, which is considered to represent the most relevant prior art, describes (the references between parentheses apply to this document): a bone system model (page 312, column 1, paragraph 2; page 313, column 2, paragraph 2) comprising osteoblasts and osteoclasts (page 313, column 2, paragraph 2) and also a mineralized matrix (page 313, column 2, paragraph 2).

2.2 The subject matter of independent claim 1 is thus novel (PCT Article 33(2)) and differs from document D1 in that the osteoblasts are placed on said mineralized matrix in such a way that a confluent carpet and/or nodules form, and the osteoclasts are placed on said carpet and/or nodules. The technical effect that ensues from this difference is, according to the inventors, the following: following the placing of the osteoclasts on the carpet of osteoblasts, said osteoclasts make their way through the contiguous population of osteoblasts. This observation thus makes it possible to validate the model as being suitable for mimicking the bone system.

2.3 Thus, the problem to be solved by the present invention can be considered to be that of: how to design a bone system which mimics the bone system?

2.4 The solution to this problem, as proposed in claim 1 of the present application, is considered to involve an inventive step (PCT Article 33(3)), for the following reasons: none of the documents cited either mentions or suggests the possibility of

designing a bone system as realized by the present

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citations and explanations supporting such statement

invention.

- 2.5 Claims 2-6 are dependent on claim 1 and as such also meet the requirements of novelty and inventive step of the PCT.

3 INDEPENDENT CLAIM 7

- 3.1 Document D1, which is considered to represent the most relevant prior art, describes (the references between parentheses apply to this document): a method of culturing (page 312, column 1, paragraph 2; page 313, column 2, paragraph 2) osteoblasts and osteoclasts (page 313, column 2, paragraph 2) with a mineralized matrix (page 313, column 2, paragraph 2).
- 3.2 The subject matter of independent claim 7 is thus novel (PCT Article 33(2)) and differs from document D1 as described in point 2.2. In addition to this difference, the subject matter differs by virtue of the fact that it is a method where the invasion of the osteoclasts through the carpet and/or the nodules of osteoblasts is observed, thus making it possible to verify whether a matrix is appropriate for use in a model which mimics the bone system. The technical effect that ensues from this difference is thus the fact the method makes it possible to verify whether a matrix is suitable for use in a model which mimics the bone system.
- 3.3 Thus, the problem that the present invention is intended to solve can be considered to be that of: how to design a method which makes it possible to identify a matrix as being suitable for use in a model which mimics the bone system?



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citations and explanations supporting such statement

3.4 The solution to this problem, as proposed in claim 7 of the present application, is considered to involve an inventive step (PCT Article 33(3)), for the same reasons as in point 2.4.

3.5 Claim 8 is dependent on claim 7 and as such also meets the requirements of novelty and inventive step of the PCT.

4 INDEPENDENT CLAIM 9

In addition to the faults mentioned in Box III, the subject matter of claim 9 is not novel and the present application does not therefore meet the requirement of novelty defined in PCT Article 33(2).

4.1 Document D1 describes (the references between parentheses apply to this document): a matrix consisting of a plate of dentine, a matrix composed of collagen and of calcium phosphate and/or calcium phosphate derivatives, preferably hydroxyapatite (page 312, column 1, paragraph 2 to column 2, paragraph 1) which can be selected by means of the method according to claim 7 or 8, as indicated in claim 9.

4.2 Document D2 describes (the references between parentheses apply to this document): a matrix consisting of a plate of dentine, a matrix composed of collagen and of calcium phosphate and/or calcium phosphate derivatives, preferably hydroxyapatite (page 135, abstract and columns 1 and 2) which can be selected by means of the method according to claims 7 or 8, as indicated in claim 9.

4.3 Document D3 describes (the references between parentheses apply to this document): a matrix

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Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability;  
citations and explanations supporting such statement

consisting of a plate of dentine, a matrix composed of collagen and of calcium phosphate and/or calcium phosphate derivatives, preferably hydroxyapatite (page 1535, abstract; page 1536, column 1, paragraphs 2 and 3) which can be selected by means of the method according to claim 7 or 8, as indicated in claim 9.

5 INDEPENDENT CLAIMS 10-14

5.1 Document D1, which is considered to represent the most relevant prior art, describes (the references between parentheses apply to this document): a bone system model (page 312, column 1, paragraph 2; page 313, column 2, paragraph 2) comprising osteoblasts and osteoclasts (page 313, column 2, paragraph 2) and also a mineralized matrix (page 313, column 2, paragraph 2).

5.2 The subject matter of claims 10-14 is thus novel (PCT Article 33(2)) and differs from document D1 as described in 2.2. Furthermore, the technical effect that ensues from this difference is also the same as that described in point 2.2. Claims 10-14 differ from one another by virtue of the fact that the model is modified so as to use it in the study of various pathologies which can affect the bone system.

5.3 Thus, the problem that the present invention is intended to solve can be considered to be that of: how to design a bone system which mimics the bone system and which can be used for the study of various bone pathologies?

5.4 Needless to say, the solution to this problem, as

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citations and explanations supporting such statement

proposed in claims 10-14 of the present application, is considered to involve an inventive step (PCT Article 33(3)), for the same reasons as those stated in point 2.4.

6 INDEPENDENT CLAIMS 15 and 17

6.1 Document D1, which is considered to represent the most relevant prior art, describes (the references between parentheses apply to this document): the use of a bone system model (page 312, column 1, paragraph 2; page 313, column 2, paragraph 2) comprising osteoblasts and osteoclasts (page 313, column 2, paragraph 2) and also a mineralized matrix (page 313, column 2, paragraph 2).

6.2 The subject matter of independent claims 15 and 17 is thus novel (PCT Article 33(2)) and differs for the same reasons as those described in point 2.2. Furthermore, the model is used for testing molecules in terms of their therapeutic or toxic effect.

6.3 Thus, the problem that the present invention is intended to solve can be considered to be that of: how to design a bone system which mimics the bone system and which can be used for studying the therapeutic or toxic effect of molecules.

6.4 Needless to say, the solution to this problem, as proposed in claims 15 and 17 of the present application, is considered to involve an inventive step (PCT Article 33(3)), for the same reasons as those stated in point 2.4.

7 INDUSTRIAL APPLICABILITY

The subject matter of claims 1-15 and 17 is considered to be industrially applicable in the

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biomedical research field.

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Box No. VII      Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Although claims 10-14 and 16 have been drafted as separate independent claims, it appears that they have the same subject matter and that they differ only by virtue of a variation in the definition of the subject matter for which protection is sought and by virtue of the terms used to defined the features thereof. Therefore, these claims are not concise and thus do not comply with the requirements of PCT Article 6.

Although claims 15 and 17 have been drafted as separate independent claims, it appears that they have the same subject matter and that they differ only by virtue of a variation in the definition of the subject matter for which protection is sought and by virtue of the terms used to defined the features thereof. Therefore, these claims are not concise and thus do not comply with the requirements of PCT Article 6.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Continuation of:

Box III

Claim 9 relates to a very large variety of products. A support within the meaning of PCT Article 6 and/or a disclosure within the meaning of PCT Article 5 can, however, only be found for a very restricted number of these products claimed. In the present case, the claim lacks support to such an extent and the disclosure of the invention in the description is so limited that a significant search covering the entire spectrum claimed is impossible. Therefore, the search was limited to the parts of the claim which have a support and a disclosure, i.e. the parts relating to the following compounds: plate of dentine, a matrix composed of collagen and of calcium phosphate and/or calcium phosphate derivatives, preferably hydroxyapatite (see page 2 of the description).

Independent claim 16 is covered by the provisions of PCT Rule 39.1 (iv) since the subject matter of the claim comprises a method of diagnosis applied to the human or animal body.

The present Authority considers that the subject matter of claim 16 is covered by the provisions of PCT Rule 67.1(iv). For this reason, no opinion will be given on the question of whether the subject matter of this claim is industrially applicable (PCT Article 34(4)(a)(i)).